Paper No. 26

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte RICHARD I. SENDEROFF, and
KATHLEEN M. KONTOR

Appeal No. 2003-0338
Application No. 08/486,451

ON BRIEF

Before WILLIAM F. SMITH, ADAMS, and GREEN, Administrative Patent Judges.

GREEN, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 21, 22, 24 and 26-37. Claims 21 and 24 are representative of the subject matter on appeal, and read as follows:

> 21. A method of stabilizing an aqueous solution of thrombopoietin comprising adding to said solution a stabilizing amount of histidine.
>
> 24. An aqueous pharmaceutical composition comprising:
>
> thrombopoietin;
>
> 10-100 mM phosphate buffer;

0.01% - 0.05% (w/v) of polysorbate 80;

an isotonic amount of sodium chloride; and
water

said composition having a pH of 6.0 ± 0.5.

The examiner relies upon the following references:

Igari et al. (Igari I)	5,344,644	Sep. 6, 1994
Igari et al. (Igari II)	5,534, 269	Jul. 9, 1996
Prestrelski et al. (Prestrelski)	5,580,856	Dec. 3, 1996

Manning, "Stability of Protein Pharmaceuticals," Pharmaceutical Research, Vol. 6, No. 11, pp. 903-918 (1989)

Claims 21, 22, 24 and 26-37 stand rejected under 35 U.S.C. § 103(a) as being obvious over the combination of Prestrelski and Manning. Claims 21, 22, 24 and 26-37 also stand rejected under 35 U.S.C. § 103(a) as being obvious over the combination of Igari I and Igari II. After careful review of the record and consideration of the issues before us, we reverse both rejections.

DISCUSSION

Claims 21, 22, 24 and 26-37 stand rejected under 35 U.S.C. § 103(a) as being obvious over the combination of Prestrelski and Manning.

Given its brevity, the entire rejection is set forth below.

> Prestrelski [ ] teach[es] the addition of several stabilizers for a number of proteins including thrombopoietin. The stabilizers used are buffers, such as citrate, acetate, phosphate and histidine, agents to maintain isotonicity, preservatives, and the same polyols as claimed herein as surfactants. These additaments are added in amounts to prevent aggregation. Amount ranges for each additive is shown. The composition is directed toward a lyophilized powder. The patent does not teach that surfactants such as polyols are used as surface adsorption inhibitors. However, this is a well known fact in the protein art, as shown by Manning [ ] at page 911, third paragraph. Therefore it would have been obvious to one of

> ordinary skill in the art to add the stabilizers shown by Prestrelski [ ] as well as add the non-ionic surfactants for their function as surface adsorption inhibitors since the reference envisions the formulation in a kit which would necessarily include vials or other vessals to contain the TPO formulation.

Paper No. 9, pages 2-3 (citations omitted).

Appellants argue that the rejection is based on improper hindsight reconstruction. See Appeal Brief, page 18. We agree.

"In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a prima facie case of obviousness. Only if that burden is met, does the burden of coming forward with evidence or argument shift to the applicant." In re Rijckaert, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993).

With respect to an obviousness rejection based on a combination of references, as the court has stated, "virtually all [inventions] are combinations of old elements." Environmental Designs, Ltd. V. Union Oil Co., 713 693, 698, 218 USPQ 865, 870 (Fed. Cir. 1983); see also Richdel, Inc. v. Sunspool Corp., 714 F.2d 1573, 1579-80, 219 U.S.P.Q. (BNA) 8, 12 (Fed. Cir. 1983) ("Most, if not all, inventions are combinations and mostly of old elements."). Therefore, an examiner may often find every element of a claimed invention in the prior art. If identification of each claimed element in the prior art were sufficient to negate patentability, very few patents would ever issue. The United States Court of Appeals for the Federal Circuit, our reviewing court, however, has stated that "the best defense against hindsight-based obviousness analysis is the rigorous application of the requirement for a showing of a teaching or motivation to

combine the prior art references." Ecolochem, Inc. v. Southern California Edison Co., 227 F.3d 1361, 1371, 56 USPQ2d 1065, 1073 (Fed. Cir. 2000). We begin our analysis with independent claim 21.

The Prestrelski reference is drawn to the formation of dried protein compositions. The reference teaches the use of a reconstitution stabilizer, wherein the reconstitution stabilizer is an excipient that prevents aggregation. The refererence then states that:

> Excipients possessing the necessary characteristics for the present invention are well-known in the art and generally function by the mechanisms of charge replusion, steric hindrance, hydrophobic binding or specific high-affinity binding to the dried protein. Exemplary excipients include various osmolytes, various salts, water soluble synthetic and natural polymers, surfactants, sulfated polysaccharides, carrier proteins, buffers and the like.

Prestrelski, column 4, lines 19-27. The reference goes on to explain that:

> Exemplary osmolytes include, but are not limited to, amino acids (e.g., histidine, salts of histidine, glycine, salts of aspartic acid, salts of glutamic acid, salts of lysine, salts of arginine, serine, praline, alanine); polyhydric alcohols (e.g. sorbitol, inositol, mannitol, xylitol and glycerol; sugars (trehalose, lactose, sucrose, glucose, galactose, maltose, mannose and fructose) and methylamines (e.g., trimethyamine-N-oxide, N,N-dimethyl-glycine, aminobutyric acid, taurine, sarcosine, betaine or salts thereof).

Id. at lines 34-43.

With respect to the proteins, Prestrelski presents a long laundry list of proteins, of which thromboprotein is just one. There is nothing in the examples or the remainder of the reference that would lead one to the combination of thrombopoeitin and histidine. A broad disclosure of a genus comprising hundreds if not thousands of protein compositions does not render any particular

species of composition that falls within the genus obvious. See In re Jones, 958 F.2d 347, 350, 21 USPQ2d 1941, 1943 (Fed. Cir. 1992); In re Baird, 16 F.3d 380, 382-83, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994).

With respect to claim 24, the rejection does not even discuss the limitations of that claim.

We note that the rejection shot-gunned all of the claims, without addressing the claims individually. For example, the rejection relies on Manning for the addition of a polyol, but a polyol is not required by independent claim 21. A claim-by-claim analysis focuses the analysis and allows for more meaningful review. Because the rejection has failed to set forth a prima facie case of obviousness, it is reversed.

Claims 21, 22, 24 and 26-37 also stand rejected under 35 U.S.C. § 103(a) as being obvious over the combination of Igari I and Igari II.

Again, due to its brevity, the entire rejection is set forth below.

> Igari [I] teach[es] that thrombopoietin is stabilized by adding to the formulation; buffers, isotonizing agents and adsorption inhibitors such as Tween 80. The patent does not teach the particular buffers claimed by the patent. Although the amino acid glycine is taught as a pH adjusting agent, histidine is not disclosed.
>
> Igari [II] disclose[s] that pH adjusting agents that can be used with thrombopoietin are glycine and histidine. Moreover they teach the addition of salts such as acetate and citrate known in the art as buffers. It would have been obvious to one of ordinary skill in the art at the time the invention was made to recognize that glycine and histidine are functional equivalents as taught by [Igari II] and to substitute one for the other and employ histidine. It would have been obvious to employ other buffers well known in the art such as those claimed herein, particularly when the secondary reference discloses the use of these with TPO.

Paper No. 9, pages 3-4 (citations omitted).

This rejection suffers from the same deficiencies as the rejection over the combination of Prestrelski and Manning. With respect to claim 21, Igari I and Igari II also teach a broad genus of protein compositions, with nothing directing the ordinary artisan to the combination of thrombopoeitin with histidine. With respect to claim 24, again, the rejection does not even discuss the limitations of that claim. Thus, this rejection is reversed for the same reasons set forth above with respect to the combination of Prestrelski and Manning.

CONCLUSION

Because neither the combination of Prestrelski and Manning, nor the combination of Igari I and Igari II, set forth a prima facie case of obviousness, the rejections set forth under 35 U.S.C. § 103(a) are reversed.

REVERSED

William F. Smith Administrative Patent Judge	))))) BOARD OF PATENT
Donald E. Adams Administrative Patent Judge	)) APPEALS AND)) INTERFERENCES
Lora M. Green Administrative Patent Judge	))

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